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WARE, TODD

ART UNIT	PAPER NUMBER
1615	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/281,430

Applicant(s)

PARIKH ET AL.

Examiner

Todd D Ware

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*-- The MAILING DATE of this communication app ars on the cover sheet with the correspond nce address --***Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status1) Responsive to communication(s) filed on 23 September 2002.2a) This action is **FINAL**. 2b) This action is non-final.3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.**Disposition of Claims**4) Claim(s) 26-53 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.6) Claim(s) 26-53 is/are rejected.7) Claim(s) _____ is/are objected to.8) Claim(s) _____ are subject to restriction and/or election requirement.**Application Papers**9) The specification is objected to by the Examiner.10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.**Priority under 35 U.S.C. §§ 119 and 120**13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).a) All b) Some * c) None of:1. Certified copies of the priority documents have been received.2. Certified copies of the priority documents have been received in Application No. _____.3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).a) The translation of the foreign language provisional application has been received.15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.**Attachment(s)**1) Notice of References Cited (PTO-892)4) Interview Summary (PTO-413) Paper No(s). _____.2) Notice of Draftsperson's Patent Drawing Review (PTO-948)5) Notice of Informal Patent Application (PTO-152)3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.6) Other: _____

DETAILED ACTION

Receipt of revocation of power of attorney filed 7-25-02 and amendment filed 9-23-02 is acknowledged. Claims 26-30 and 34-38 have been amended and new claims 39-53 have been added as requested. Claims 26-53 are pending.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. **Claims 26-33 and 36-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauer et al (5,342,625; hereafter '625) in view of Hamied et al (5,929,030; hereafter '030) or vice versa.**
3. '625 teaches a non-aqueous, microemulsion pre-concentrate composition comprising a hydrophobic or water insoluble agent such as cyclosporin, 10 to 80% of a hydrophobic component (C 8, L 58- C 9, L39 and examples), 20 to 80% of a surfactant phase (C 9, L 40- C 12, L 6 and examples) and a hydrophilic component, such as ethanol and/or 1,2 propylene glycol. '625 teaches that the particle size of the microemulsions obtainable from the pre-concentrate is about 150-2000 Å (15-200 nm) when added to water.
4. '030 teaches microemulsion formulations for water insoluble active substances such as taxol, 20-80% of a hydrophobic oil phase, 1-60% of a surfactant phase, and 15-75% of a hydrophilic phase.

5. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine '625 and '030 with the motivation of enhancing the resorption/bioavailability of taxol and the expectation that microemulsions provide increased resorption/bioavailability over non-microemulsion formulations, as taught by '625. Furthermore, motivation is also provided in '030 which teaches that such compositions do not form solid microfine active agent after administration. Thus, the expectation is that such a formulation would not precipitate taxol after administration.

6. **Claims 26-33 and 36-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauer et al (5,342,625; hereafter '625) in combination with Hamied et al (5,929,030; hereafter '030) and further in combination with Rathi et al (6,004,573; hereafter '573) or Hamied et al (5,929,030; hereafter '030) in combination with Hauer et al (5,342,625; hereafter '625) and further in combination with Rathi et al (6,004,573; hereafter '573).**

7. '625 and '030 are relied upon for all that they teach as stated previously.

8. '573 is relied upon to further reinforcing the similar dissolution properties of cyclosporin and taxol, stating that they are both hydrophobic agents.

9. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine '625 and '030 with the motivation of enhancing the resorption/bioavailability of taxol and the expectation that microemulsions provide increased resorption/bioavailability over non-microemulsion formulations, as taught by '625, for hydrophobic active agents. Furthermore, motivation is also provided in '030

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which teaches that such compositions do not form solid microfine active agent after administration. Thus, the expectation is that such a formulation would not precipitate hydrophobic active agent such as taxol after administration.

10. **Claims 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauer et al (5,342,625; hereafter '625) in combination with Hamied et al (5,929,030; hereafter '030) and further in combination with Sime et al (WO 96/35415; hereafter '415).or Hamied et al (5,929,030; hereafter '030) in combination with Hauer et al (5,342,625; hereafter '625) and further in combination with Sime et al (WO 96/35415; hereafter '415).**

11. '625 and '030 are relied upon for all that they teach as stated previously.

12. '415 is relied upon for teaching compositions comprising grapefruit extract and taxol to inhibit cytochrome P450 enzyme and decrease metabolism/increasing stability of the taxol.

13. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to include grapefruit extract in a taxol microemulsion with the motivation of decreasing metabolism/increasing stability of the taxol.

14. **Claims 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hauer et al (5,342,625; hereafter '625) in combination with Hamied et al (5,929,030; hereafter '030) in combination with Rathi et al (6,004,573; hereafter '573) and further in combination with Sime et al (WO 96/35415; hereafter '415) or**

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Hamied et al (5,929,030; hereafter '030) in combination with Hauer et al (5,342,625; hereafter '625) in combination with Rathi et al (6,004,573; hereafter '573) and further in combination with Sime et al (WO 96/35415; hereafter '415).

15. '625, '030, and '573 are relied upon for all that they teach as stated previously.

16. '415 is relied upon for teaching compositions comprising grapefruit extract and taxol to inhibit cytochrome P450 enzyme and decrease metabolism/increasing stability of the taxol.

17. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to include grapefruit extract in a taxol microemulsion with the motivation of decreasing metabolism/increasing stability of the taxol.

Response to Arguments

18. Applicant's arguments filed 9-23-02 have been fully considered but they are not persuasive. Applicant argues that Hauer is directed toward cyclosporin formulations and does not teach a taxanes or that the composition is a preconcentrate or that the formulations are oral or parenterally administered. In response, applicant is first directed to the abstract and Example 1 of Hauer which state that administration of the formulation includes oral pre-concentrate dosage forms. It is agreed Hauer does not teach a taxanes. In response, the Examiner points to Hamied which teaches that both cyclosporin and taxol are hydrophobic and therefore suggests the equivalency of the compounds. Therefore, the Examiner has met the burden.

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19. Applicant also argues that the instant claims state that the surfactant consists of one or more non-ionic surfactants and that lecithin is an ionic surfactant. In response, Hamied teaches mixtures of surfactants such as polyoxyethylene-sorbitan monooleate and lecithin. Polyoxyethylene-sorbitan monooleate is a non-ionic surfactant and the claims recite comprising language. The claims also recite consisting essentially of language when referring to the carrier and for the purposes of examining and searching this is considered equivalent to comprising (MPEP 2111.03, *PPG Industries v. Guardian Industries*, 48 USPQ2d 1355) since applicant has not shown that the introduction of additional steps or components would be detrimental to applicant's invention.

Furthermore, applicant is directed to Merck Index which shows lecithin as being non-ionic.

20. Applicant also argues that Hamied specifically teaches away from applicant's invention since Hamied teaches that the formulation of Hamied is free from ethanol. The instant claims require "up to" a particular percentage of a hydrophilic component (i.e. up to 40%). The phrase "up to" includes 0%. Thus, the claims do not require a hydrophilic component.

21. Applicant then argues that the references do not disclose the particular percentage of taxanes bioavailability. However, increase in bioavailability is the purpose of Hauer (see column 5, lines 14-20) and the motivation of the rejection for combining the references. Accordingly, the burden is shifted to applicant to demonstrate the criticality of the instant claims and the rejection is maintained.

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Conclusion

22. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Todd D Ware whose telephone number is (703) 305-1700. The examiner can normally be reached on M-F, 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703)308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

G S Kishore
Gollamudi S. Kishore, PhD
Primary Examiner
Group 1500

tw
December 16, 2002